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(54) Title: XANTHONES, THIOXANTHONES AND ACRIDINONES AS DNA-PK INHIBITORS

(57) Abstract: Compound that inhibit DNA-dependent protein kinase, compositions comprising the compounds, methods of inhibiting the DNA-PK biological activity, methods of sensitizing cells the agents that cause DNA lesions, and methods of potentiating cancer treatment are disclosed.

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Relevant to claim No.

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D311/86 C07D405/04 C07D219/06 C07D219/16 C07D401/06
C07F9/655 C07F9/64 C07D405/12 C07D471/04 A61K31/35
A61P35/00 //(C07D471/04,221:00,221:00)

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B. FIELDS SEARCHED

Category °

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07D C07F A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

Citation of document, with indication, where appropriate, of the relevant passages

EPO-Internal, WPI Data, BEILSTEIN Data, EMBASE, BIOSIS, CHEM ABS Data, PAJ

	l		
х	WO 02/20500 A (ICOS CORP) 14 March 2002 (2002-03-14)		1-8, 11-21, 23-45
Α	claim 1		9,10,22
X	ABADI ASHRAF H ET AL: "Synthesiantitumor and antitubercular evacertain new xanthenone and acridanalogs" ARZNEIMITTEL-FORSCHUNG, vol. 49, no. 3, March 1999 (1999-pages 259-266, XP002296342 ISSN: 0004-4172 page 263	luation of inone	1-8, 11-19, 23-45
X Furt	her documents are listed in the continuation of box C.	Patent family members are listed	in annex.
"A" docume consider in the consideration in the considera	ent defining the general state of the art which is not dered to be of particular relevance document but published on or after the international tate ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another n or other special reason (as specified) ent referring to an oral disclosure, use, exhibition or means ent published prior to the international filing date but han the priority date claimed	"T" later document published after the integration or priority date and not in conflict with cited to understand the principle or the invention. "X" document of particular relevance; the cannot be considered novel or cannot involve an inventive step when the decannot be considered to involve an indocument is combined with one or ments, such combination being obvious in the art. "&" document member of the same patent.	the application but eory underlying the claimed invention to be considered to cournent is taken alone claimed invention eventive step when the ore other such docu-
Date of the	actual completion of the international search	Date of mailing of the international sea	arch report
1	5 September 2004	11/10/2004	
Name and	mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Authorized officer Steendijk, M	

Ini tional Application No PCT/US2004/008459

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	WO 92/16517 A (XENOVA LTD) 1 October 1992 (1992-10-01) claim 1	1-8, 11-19, 23-45
X	MARI STEFANIA ET AL: "Flavone and xanthone derivatives related to fluoroquinolones" FARMACO (LAUSANNE), vol. 54, no. 6, 30 June 1999 (1999-06-30), pages 411-415, XP002296343 ISSN: 0014-827X page 412 -page 413	1-8, 11-19,23
X	DE 31 41 970 A (VNII LEKARSTVENNYCH RASTENIJ V) 5 May 1983 (1983-05-05) claim 1	1-8, 11-19,23
X	WO 96/16632 A (ROBIN JEAN RENAUD ; ROCHER YVES BIOLOG VEGETALE (FR); ROUILLARD FRANCO) 6 June 1996 (1996-06-06) claim 1	1-8, 11-19,23
X	DATABASE CAPLUS 'Online! STN; 1989 KLOPMAN ET AL.: "An artificial inteligence approach" Database accession no. 1989:150323 XP002296348 see TRN: 119427-89-3, 119427-90-6 abstract & MOLECULAR PHARMACOLOGY, vol. 34, no. 6, 1988, pages 852-862,	1-8, 11-19,23
X	WO 01/17985 A (VALENTI PIERO ; INDENA SPA (IT); BOMBARDELLI EZIO (IT)) 15 March 2001 (2001-03-15) claim 1	11-19, 23-45
X	US 2001/027210 A1 (WILSON WILLIAM R) 4 October 2001 (2001-10-04) column 1	11-19, 23-45
X	GHOSH CHANDRA KANTA ET AL: "Benzopyrans: Part 30. Synthesis of substituted xanthones from 3-acyl-2-methylbenzopyran-4-ones" TETRAHEDRON, vol. 49, no. 19, 1993, pages 4127-4134, XP002296344 ISSN: 0040-4020 page 4128	1-9

tional Application No PCT/US2004/008459

C (C	POOLINE TO CONCERN TO DE DEL ENAME	PCT/US2004/008459		
Category •	ation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	DATABASE CAPLUS 'Online! STN; 2002 XUAN ET AL.: "Two new O and C-glycosylxanthones" Database accession no. 2002:80848 XP002296349 see RN: 400759-79-7 abstract & GAODEN XUEXIAO HUAXUE XUEBAO, vol. 22, no. 10, supp., 2001, pages 148-150,	1-9		
X	FONTENEAU NADIA ET AL: "Synthesis of quinone and xanthone analogs of rhein" TETRAHEDRON, vol. 57, no. 44, 29 October 2001 (2001-10-29), pages 9131-9135, XP002296345 ISSN: 0040-4020 page 9133	1-9		
X	DATABASE CAPLUS 'Online! STN; 1973 AGASIMUNDIN ET AL.: "Furano compounds" Database accession no. 1973:124471 XP002296350 see RN: 41534-30-9 abstract & JOURNAL FUER PRAKTISCHE CHEMIE, vol. 314, no. 3-4, 1972, pages 507-514,	11-21		
X	DATABASE CAPLUS 'Online! STN; 1969 GOUD ET AL.: "Furan compounds. XVI" Database accession no. 1969:96661 XP002296351 see RN: 22315-95-3 abstract & MONATSH. CHEM., vol. 100, no. 1, 1969, pages 38-41,	11-21		
X	EP 0 471 516 A (ICI PLC) 19 February 1992 (1992-02-19) claim 1	1-8, 11-19, 23-45		
X	WO 90/14008 A (SLOAN KETTERING INST CANCER) 29 November 1990 (1990-11-29) claim 1	11-19, 23-45		

Int onal Application No
PCT/US2004/008459

Relevant to claim No. 1-8, 11-19, 23	
1-8,	
1-8, 11-19,23	
1-8, 11-19, 23-45	
1-8, 11-19,23	
11-21, 23-45	
11-21, 23-45	
1-8, 11-19,23	

In: Ional Application No PCT/US2004/008459

		PCT/US2004/008459
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate of the relevant passages	Palevant to claim No.
Jaredor A	Onation of determine, with includation, where appropriate, of the relevant passages	neievant to ciaim No.
X X	Citation of document, with indication, where appropriate, of the relevant passages HARFENIST M ET AL: "SELECTIVE INHIBITORS OF MONOAMINE OXIDASE. 3. STRUCTURE-ACTIVITY RELATIONSHIP OF TRICYCLICS BEARING IMIDAZOLINE, OXADIAZOLE, OR TETRAZOLE GROUPS" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 39, no. 9, 1996, pages 1857–1863, XP001097214 ISSN: 0022-2623 the whole document	1,3-8, 11-19,23

formation on patent family members

Int onal Application No PCT/US2004/008459

				PCT/US2004/008459		
Patent document cited in search report		Publication date		Patent family member(s)	Publication date	
WO 0220500	Α	14-03-2002	AU	8843201 A	22-03-2002	
			EP	1351946 A2	15-10-2003	
			WO	0220500 A2	14-03-2002	
			US	2002165218 A1	07-11-2002	
WO 9216517	Α	01-10-1992	EP	0580609 A1	02-02-1994	
			WO	9216517 A1	01-10-1992	
			GB	2269382 A ,B	09-02-1994	
			JP	6506202 T	14-07-1994 	
DE 3141970	Α	05-05-1983	GB	2108383 A ,B	18-05-1983	
			DE	3141970 A1	05-05 - 1983	
WO 9616632	A	06-06-1996	FR	2727313 A1	31-05-1996	
			FR	2731906 A1	27-09-1996	
			FR	2735695 A1	27-12-1996	
			AT AU	206611 T 4264396 A	15-10-2001	
			CA	2180745 A1	19-06-1996 06-06-1996	
			DE	69523169 D1	15-11-2001	
			DE	69523169 T2	16-05-2002	
			ĒΡ	0793476 A1	10-09-1997	
			WO	9616632 A1	06-06-1996	
			JP	2858961 B2	17-02-1999	
			JP	9506906 T	08-07-1997	
			NO	963053 A	20-09-1996	
			PL	315636 A1	25-11-1996	
			US 	5824320 A	20-10-1998	
WO 0117985	Α	15-03-2001	AT	236147 T	15-04-2003	
			AU AU	775790 B2 7000000 A	12-08-2004	
4			CA	2382129 A1	10-04-2001 15-03-2001	
			CN	1371371 T	25-09-2002	
			CZ	20020785 A3	12-06-2002	
			DE	60001974 D1	08-05-2003	
			DE	60001974 T2	19-02-2004	
			DK	1212312 T3	21-07-2003	
			MO	0117985 A1	15-03-2001	
			EP	1212312 A1	12-06-2002	
			ES	2195933 T3	16-12-2003	
			HK HU	1043368 A1 0202578 A2	15-08-2003	
			JP	2003 5 08 5 24 T	28-11-2002 04-03-2003	
			NO	2003308324 T	03-05-2003	
			PL	356699 A1	28-06-2004	
			PΤ	1212312 T	29-08-2003	
			SI	1212312 T1	31-12-2003	
			SK	3092002 A3	07-10-2003	
			US ————	2002183318 A1	05-12-2002	
US 2001027210	A1	04-10-2001	JP	2001247459 A	11-09-2001	
EP 0471516	Α	19-02-1992	ΑU	8142291 A	20-02-1992	
			CA	2048298 A1	17-02-1992	
			CS EP	9102510 A3	18-03-1992	
				31/1 / 1 h l h N T	しゅーハク1ののク	
			FΙ	0471516 A1 913893 A	19-02-1992 17-02-1992	

formation on patent family members

In: onal Application No PC1/US2004/008459

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
EP 0471516	A		HU IE JP MX NO PT ZA	58293 A2 912616 A1 4257563 A 9100703 A1 913187 A 98680 A 9105937 A	28-02-1992 26-02-1992 11-09-1992 01-04-1992 17-02-1992 31-08-1992 29-04-1992
WO 9014008	A	29-11-1990	AU US WO	5831090 A 5340818 A 9014008 A1	18-12-1990 23-08-1994 29-11-1990
JP 11199565	Α	27-07-1999	NONE		
US 4539412	A	03-09-1985	NONE		
US 3904631	Α	09-09-1975	GB PH	1434878 A 10283 A	05-05-1976 05-11-1976